REMARKS

Upon entry of this amendment, claims 37 to 52 are pending. Applicant has cancelled claims 2, 4 to 8, 18 to 21 and 27 to 36, and added new claims 37 to 52. Applicant reserves the right to pursue any subject matter removed by these amendments in one or more continuation applications. New claim 37 is in independent form. The remaining claims (i.e. claims 38-52) ultimately depend from claim 37.

New claim 37 is supported by the working examples in the application, where it is demonstrated both *in vivo* (in guinea pigs and sheep) and on mammalian (guinea pig and human) airway tissue *in vitro* that CGRP is effective at reducing a number of airway responses, such as airway constriction (Examples 1 and 2), airway spasm (Example 2), airway hyperreactivity (Example 4), eosinophil accumulation in bronchial walls (Example 3) and airway resistance (Examples 2 and 4), with no significant haemodynamic side effects (Example 4).

In the working examples, it is demonstrated in the instant application that CGRP and its linear analogs confer a protective effect in tissues or subjects prone to or at risk of experiencing such airway responses (e.g. allergic subjects), in that its administration prior to such airway responses reduces their severity or prevents their occurrence altogether. A significant advantage of using CGRP for the reduction of such airway responses is that it does not result in any significant haemodynamic side effects, as demonstrated in the working examples.

The dependent claims are supported, for example, as follows:

Claim(s)	Support
38-40	Examples 1-4
41	page 38, line 23
42	page 26, lines 21-22
43-47	former claims 33, 35, 34, 36 and 2, respectively
48	Examples 3 and 4
49	page 23, lines 6-7
50-52	former claims 18-20

Concerning 35 USC § 102

Claims 2, 4-8, 18-21, 27-28 and 31-34 of record stand rejected pursuant to 35 USC § 102(e) as being anticipated by United States Patent No. 5,858,978 to Vignery as evidenced by *The Merck Manual*. The Examiner states that "the use of CGRP to treat asthma is

specifically named" (Paper No. 24). Applicant respectfully submits that the presently amended claims patentably distinguish from Vignery.

New claim 37 is directed to a method of reducing a stimulus-induced airway response, comprising:

administering to a subject at risk of experiencing a stimulus-induced airway response a therapeutically effective amount of an agent selected from the group consisting of:

(a) human calcitonin gene-related peptide (human CGRP);

(b) rat CGRP;

(c) the diacetoamidomethyl cysteine form of (a); and

(d) the diacetoamidomethyl cysteine form of (b);

wherein said agent is administered prior to said airway response and wherein said method results in no or substantially no haemodynamic side effects.

Applicant respectfully submits that Vignery makes no mention of stimulus-induced airway responses. Most significantly, Vignery does not teach or suggest that any of the agents mentioned in sections (a)-(d) of claim 37 can be administered to a subject at risk of experiencing a stimulus-induced airway response, prior to an airway response, without haemodynamic side effects, as instantly claimed.

As shown in the working examples, Applicant has discovered that the administration of CGRP does not significantly affect airway properties in the absence of a stimulus-induced response, as noted for example on pages 26 (lines 4-7) and 29 (lines 28-29). Further, Applicant has discovered that the administration of CGRP does not result in any significant haemodynamic side effects (e.g. changes in heart rate and/or blood pressure; see Figure 8B), in contrast to drugs such as salbutamol which do have effects on such parameters (see Figure 8A).

Thus, in accordance with the present invention, it is possible and advantageous to administer the agents recited in claim 37 prior to airway response, without significant haemodynamic side effects. These advantages, discovered by Applicant, thus make CGRP conducive to a pre-treatment-based "protective" use, via administration prior to an airway response, without undesirable changes in e.g. heart rate and/or blood pressure.

Vignery does not teach that CGRP does not significantly affect airway properties in the absence of a stimulus-induced response and does not teach administering CGRP prior to airway response, as instantly claimed. Therefore, the instant claims are novel over Vignery as evidenced by *The Merck Manual*.

Moreover, prior to the present invention, based on what was known about drugs such as salbutamol, the skilled person would not have expected that CGRP would not affect baseline haemodynamic characteristics in a subject prior to airway response. Therefore, the skilled person would not be motivated to administer CGRP prior to airway response (as presently claimed), in view of the expectation of negative haemodynamic side effects. Only Applicant's discovery of the lack of effect of CGRP on baseline haemodynamic parameters makes administration of CGRP prior to airway response a viable treatment method. For these reasons, the instant claims are also unobvious over Vignery as evidenced by *The Merck Manual*.

It is believed this responds to all of the Examiner's concerns, however, if the Examiner has any further questions, he is invited to contact David Schwartz (Reg. No. 48,211) at 613-232-2486. Further, If the Examiner does not consider that the application is in a form for allowance, an interview with the Examiner is respectfully requested.

Respectfully submitted,

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Date

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